REMARKS

Claims 1-41 are pending in this application. Claims 4, 5, 9-14, 17, 19-22, 24-27, 35-37 and 41 are amended herein to better conform with the requirements of U.S. practice. Claims 1-3, 6-8, 15, 16, 18, 23, 26-34 and 38-40 remain unchanged.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants submit that this application is now in condition for allowance. Early favorable action is solicited. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: July 11, 2002

Timothy A. French
Reg. No. 30,175

Fish & Richardson P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

20412016.doc

Version with markings to show changes made

In the specification:

Paragraph beginning at page 19, line 16 has been amended as follows:

--Figure [10] 10a illustrates ELISA titres of antibodies to *L3 galE* LPS (IgG) in paired sera taken early and late from children with invasive meningococcal disease, and Figure 10b illustrates means % phagocytosis of *Neisseria meningitidis* MC58 with paired sera taken early and late from children with invasive meningococcal disease with human peripheral blood mononuclear cells and human complement; --

Paragraph beginning at page 55, line 7 has been amended as follows:

--We present data on three paired sera taken from infants early (acute) and later (convalescent) during culture confirmed invasive meningococcal disease (IMD) that resulted from infection with *Neisseria meningitidis* isolates of immunotypes L1, L3 (MAb b5 reactive) (patients 1 and 2) and L2 immunotype (MAb B5 non-reactive) (patient 3) [(Figure 10)] (Figures 10a and 10b). The *Neisseria meningitidis* isolates for patients 1, 2, 3 were L1 (B nt pl.14), L3 (B15 p1.7) and L2 (C2a p1.5) respectively. One paired sera from patient 2 infected with a *Neisseria meningitidis* strain that was MAb B5 reactive demonstrated an increase in specific inner core LPS antibodies by ELISA between early and late infection (p=0.03 not significant two-tailed paired t-test, 95% CI 0.09-90.8)) (Figure 10a). Patient 1 sera demonstrated no significant difference in the titre of antibody taken early and later during IMD but the titre of the early sample was already at a high level (Figure 10a). The lack of increase may reflect higher affinity antibody in the convalescent sample that would not be detected in this ELISA. However in both patient 1 and 2 sera there was a nearly significant increase in functional activity in the convalescent sera in an opsonophagocytosis assay with L3 wild-type strain MC58 and human peripheral polymorphonuclear cells (p=0.06 two-tailed pared t-test, 95%CI 0.90-5.96) (Figure 10b) (Plested *et al.* 2000b). There was no significant increase in specific antibody titre between acute and convalescent sera taken from patient 3 infected with L2 immunotype strain (MAb B5 non-reactive) as measured by ELISA (Figure 10a). There was no significant functional activity in

OP assay against L3 wild-type strain with sera taken from patient 3 early or later during IMD (Figure 10b). This demonstrates the clinical relevance of the MAb B5 epitope *in vivo* and that specific inner core LPS antibodies are functional *in vivo*.--

Paragraph beginning at page 56, line 1 has been amended as follows:

--Figure [10. A] 10a. ELISA titres of antibodies to L3 *galE* LPS (lgG) in paired sera taken early and late from children with invasive meningococcal disease.--

Paragraph beginning at page 56, line 3 has been amended as follows:

--Figure 10b [B]. Mean % phagocytosis of *Neisseria meningitidis* MC58 with paired sera taken early and late from children with invasive meningococcal disease with human peripheral blood mononuclear cells and human complement.--

In the claims:

Claims 4, 5, 9-14, 17, 19-22, 24-27, 35-37 and 41 have been amended as follows:

--4. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component is substantially free from outer core lipopolysaccharide.--

--5. (Amended) A vaccine according to [any preceding] claim 1, wherein the species of the pathogenic *Neisseria* is *Neisseria meningitidis*.--

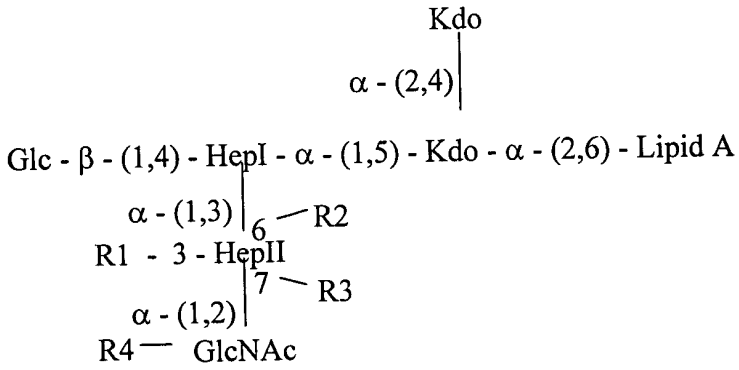
--9. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component comprises of or consists of an epitope which is a part or all of the inner core structure of a *Neisseria* LPS, is derived from this inner core, is a synthetic version of the inner core, or is a functional equivalent thereof.--

--10. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component is an epitope on the LPS inner core [characterised] characterized by the presence of a phosphoethanolamine moiety linked to the 3-position at HepII of the inner core, or is a functional equivalent thereof.--

--11. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component is an epitope on the LPS inner core which comprises a glucose residue at HepI.--

--12. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component is an epitope on the LPS inner core which comprises an N-acetyl glucosamine at HepII of the inner core LPS.--

--13. (Amended) A vaccine according to [any preceding] claim 1, wherein the inner core LPS consists of an inner core oligosaccharide attached to lipid A, with the general formula as shown:



where R1 is a substituent at the 3-position of HepII, and is hydrogen or Glc-α-(1, or phosphoethanolamine; R2 is a substituent at the 6-position of HepII, and is hydrogen or phosphoethanolamine; R3 is a substituent at the 7-position of HepII, and is hydrogen or phosphoethanolamine, and R4 is acetyl or hydrogen at the 3-position, 4-position or 6-position of the GlcNAc residue, or any combination thereof; and where Glc is D-glucopyranose; Kdo is 3-deoxy-D-*manno*-2-octulosonic acid; Hep is L-*glycero*-D-*manno*-heptose, and GlcNAc is 2-acetamido-2-deoxy-D-glucopyranose.--

--14. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic component is reactive with the B5 antibody produced by the hybridoma deposited under accession number IDAC 260900-1.--

--17. (Amended) A vaccine according to claim 15 [or 16], wherein the said few immunogenic components elicit functional antibodies in at least 85% of the strains within the species of the pathogenic *Neisseria*.--

--19. (Amended) A vaccine according to [any of the claims] claim 15 [to 18], wherein an immunogenic component is reactive with the A4 antibody produced by the hybridoma deposited under accession number IDAC 260900-2.--

--20. (Amended) A vaccine according to [any preceding] claim 1, wherein the immunogenic element of the vaccine is an epitope accessible on the bacterium in the presence of bacterial capsule.--

--21. (Amended) A vaccine according to [any preceding] claim 1, comprising one or more immunogen components which are capable of stimulating antibodies which are opsonic.--

--22. (Amended) A vaccine according to [any preceding] claim 1 for the treatment of *Neisseria meningitidis*.--

--24. (Amended) A vaccine according to [any preceding] claim 1 for the prevention of meningitis, septicaemia or pneumonia or other manifestation of systemic or local disease occasioned by *Neisseria meningitidis*.--

--25. (Amended) A vaccine according to [any of the claims] claim 1 [to 22] for the treatment of urethritis, salpingitis, cervicitis, proctitis, pharyngitis, pelvic inflammatory disease or other manifestation of systemic or local disease occasioned by *Neisseria gonorrhoeae*.--

--26. (Amended) A vaccine according to [any preceding] claim 1 which is a conjugated vaccine.--

--27. (Amended) A vaccine according to [any preceding] claim 1, which is derived from a commensal *Neisseria*.--

--35. (Amended) A pharmaceutical preparation comprising an antibody according to [any of claims] claim 29 [to 32] in combination with a pharmaceutically acceptable carrier.--

--36. (Amended) A method for the treatment of *Neisseria* infection, the method comprising administering to a subject in need of such treatment an effective amount of a vaccine according to [any of claims] claim 1 [to 28].--

--37. (Amended) A method for the treatment of *Neisseria* infection, the method comprising administering to a subject in need of such treatment an effective amount of an antibody according to [any of claims] claim 28 [to 31].--

--41. (Amended) Use of an antibody according to [any of claims] claim 29 [to 32] in the preparation of a medicament for the treatment of *Neisseria* infection.--